Proposed Revised Claims for 1275/190

1. (once amended) A method of providing an iron oxide complex for administration to a mammalian subject, the method [~~comprising~~] consisting of:
producing a carboxyalkylated reduced polysaccharide iron oxide complex; and
sterilizing the complex by autoclaving.

2. (no change) A method according to claim 1, wherein the reduced polysaccharide is a reduced polymer of glucose.

3. (no change) A method according to claim 2, wherein the reduced polymer of glucose is a reduced dextran.

4. (no change) A method according to claim 1, wherein the reduced polysaccharide is produced by reacting a polysaccharide with a reagent selected from the group consisting of: a borohydride salt, and hydrogen in the present of an hydrogenation catalyst.

5. (cancel) A method of providing an iron oxide complex for administration to a mammalian subject, the method comprising:
producing a derivatized reduced polysaccharide iron oxide complex; and
sterilizing the complex by autoclaving.

6. (cancel) A method according to claim 5, wherein producing the complex includes derivatizing a reduced polysaccharide by carboxyalkylation.

7. (once amended) A method according to claim [6] 1, wherein [~~the carboxyalkylation is a carboxymethylation~~] producing the complex includes carboxyalkylating a reduced polysaccharide by carboxymethylation.

8. (no change) A method according to claim 7, wherein the reduced polysaccharide is a reduced dextran.

9. (no change) A method according to claim 8, wherein the administration to a mammalian subject is administration to a human.

10. (once amended) A method according to claim [~~5~~] 1, wherein the [~~derivatized~~] carboxyalkylated, reduced polysaccharide isolated as [~~the~~] a sodium salt does not contain an infrared absorption peak in the region of about 1650 cm^{-1} to about 1800 cm^{-1}.

11. (once amended) A method according to claim [~~5~~] 1, wherein producing the [~~derivatized~~] carboxyalkylated reduced polysaccharide is achieved at a temperature of less than about 50 °C.

12. (once amended) A method according to claim 11, wherein producing the [~~derivatized~~] carboxyalkylated reduced polysaccharide is achieved at a temperature of less than about 40 °C.

13. A method according to claim [~~5~~] 1, wherein the iron oxide is superparamagnetic

18. A reduced polysaccharide iron oxide complex produced according to the method of claim 1, wherein the produced [~~such~~] complex [~~being~~] is stable at a temperature of at least 100 °C.

19. (once amended) A reduced polysaccharide iron oxide complex according to claim 18, [~~such~~] wherein the produced complex [~~being~~] is stable at a temperature of about 121 °C.

20. (once amended) A reduced polysaccharide iron oxide complex according to claim 19, [~~such~~] wherein the produced complex [~~being~~] is stable at a temperature of at least about 121 °C for a period of time effective to sterilize the complex.

21. (cancel) A reduced polysaccharide iron oxide complex according to claim 18, wherein the reduced polysaccharide is derivatized.

22. (once amended) A reduced polysaccharide iron oxide complex according to claim [~~21~~] 18, wherein the [~~derivatized~~] carboxyalkylated reduced polysaccharide is selected from the group consisting of a [~~carboxyalkyl~~] carboxymethyl, carboxyethyl and carboxypropyl reduced polysaccharide.

23. (cancel) A reduced polysaccharide iron oxide complex according to claim 22, wherein the carboxyalkyl is selected from the group consisting of carboxymethyl, carboxyethyl, and carboxypropyl.

24. (once amended) A reduced polysaccharide iron oxide complex according to claim [~~23~~] 22, wherein the reduced polysaccharide is a reduced dextran.

25. (once amended) A reduced polysaccharide iron complex according to claim 22, wherein the [~~derivatized~~] carboxyalkylated reduced dextran is a carboxymethyl reduced dextran.

26. (twice amended) A reduced polysaccharide iron oxide complex according to claim 24, wherein [~~the amount of derivatization of~~] the carboxyalkylated reduced dextran [~~is~~] comprises at least about 750 micromole of carboxyl groups per gram of polysaccharide.

27. (twice amended) A reduced polysaccharide iron oxide complex according to claim 26, wherein [~~the level of derivatization of~~] the carboxyalkylated reduced dextran [~~is~~] comprises at least about 900 micromole of carboxyl groups per gram of polysaccharide.

28. (twice amended) A reduced polysaccharide iron oxide complex according to claim 27, wherein [~~the amount of derivatization of~~] the carboxyalkylated reduced dextran [~~is~~] comprises at least about 1,10 micromole of carboxyl groups per gram of polysaccharide.

29. (twice amended) A reduced polysaccharide iron oxide complex according to claim [~~26~~] 28, wherein [~~the amount of derivatization of~~] the carboxyalkylated reduced dextran [~~is~~] comprises [at least] less than about 1500 micromole of carboxyl groups per gram of polysaccharide[~~, wherein said complex remains a colloidal suspension without substantial aggregation~~] wherein said complex does not form substantial particulates.

Restrict

35. (thrice amended) An improved method of administering to a mammalian subject a polysaccharide iron oxide complex [~~of the type wherein there is a risk of edematous response~~], wherein the improvement comprises [~~utilizing for administration a derivatized~~] administering a carboxyalkylated reduced polysaccharide [~~composition~~] iron oxide complex [~~and in derivatizing the polysaccharide, providing~~] having an extent of [~~derivatization~~] carboxyalkylation sufficient to produce decreased edematous response to the [~~derivatized composition so that there is a decreased edematous response~~] carboxyalkylated complex in comparison to [~~utilizing a~~] an edematous response to an administered polysaccharide that has not been thus [~~derivatized~~] carboxyalkylated.

no autoclaving

36. (thrice amended) An improved method of administering to a mammalian subject a polysaccharide iron oxide complex wherein the [~~composition includes~~] polysaccharide in the complex is dextran [~~of the type wherein there is a risk of edematous response~~], wherein the improvement comprises [~~utilizing for administration a carboxyalkylated~~] administering a carboxymethylated reduced dextran [~~in lieu of dextran~~] iron oxide complex [~~and in carboxymethylating the dextran, providing~~] having an extent of carboxymethylation sufficient to produce decreased edematous response to the [~~derivatized composition so that there is a decreased edematous response~~] carboxymethylated complex in comparison to [~~utilizing a~~] an edematous response to an administered dextran that has not been thus [~~derivatized~~] carboxymethylated.

no autoclaving

39 (twice amended) A method according to claim 36, further comprising sterilizing the [~~composition~~] complex by autoclaving.

40. (cancel) A method according to claim 39, wherein the subject is in need of a plasma extender.

41. ([redacted]) A method according to claim 36, further comprising providing a solution of an iron salt to form a carboxymethylated reduced dextran iron colloid formulation producing decreased edematous response.

42. (twice amended) A method according to claim [~~41~~] 36, further comprising sterilizing the carboxymethylated reduced dextran iron [~~formulation~~] oxide complex by autoclaving.

43. (no change) A method according to claim 42, wherein the subject is in need of iron.

44. (no change) A method according to claim 43, wherein the subject in need of iron is selected from the group of: a cancer patient, a gastroenteritis patient, and an erythropoietin recipient.

45. (thrice amended) A method of magnetic resonance imaging (MRI) according to claim [~~41 of magnetic resonance imaging (MRI)~~] 36 of the type including a reduced polysaccharide[~~-derived~~] iron oxide MRI contrast agent, [~~wherein there is a risk of edematous response~~], wherein the improvement comprises administering to the subject an effective dose of the contrast agent to [~~obtain~~] facilitate magnetic resonance imaging (MRI) of a tissue or organ [~~so that~~] wherein there is a decreased edematous response in comparison to [utilizing] an edematous response when an unmodified polysaccharide contrast agent is administered.

46. (twice amended) A method of magnetic resonance imaging according to claim 45, wherein the improvement further comprises administering [~~an effective dose of the agent to obtain an MRI, followed within a single clinical visit by administering a further effective dose, to obtain a further MRI~~] successive effective doses of the contrast agent to facilitate successive magnetic resonance imaging of a tissue or organ.

47. (once amended) A method according to [~~either of claims 46~~] claim 45, wherein the effective dose is about 0.1 to about 4.0mg of iron per kg of body weight of the subject.

48. (no change) A method according to claim 47, wherein the effective dose is about 0.2 to about 0.6 mg of iron per kg of body weight.

49. (no change) A method according to claim 47, wherein the effective dose is about 0.4 to about 1.0 mg of iron per kg of body weight.

50. (no change) A method according to claim 47, wherein the effective dose is about 1.0 to about 4.0 mg of iron per kg of body weight.

51. (once amended) A method according to claim 46, wherein the [~~interval between administering~~] successive effective doses [~~and administering the further effective dose is~~] are administered less than one hour apart.

52. (once amended) A method according to claim 51, wherein the [~~interval between administering~~] successive effective doses [~~and administering the further effective dose is~~] are administered less than thirty minutes apart.

53. (no change) A method of providing a contrast agent for in vivo MRI of a subject, comprising the steps of:

formulating a composition which is a carboxymethylated reduced coated ultrasmall superparamagnetic iron oxide colloid; and

terminally sterilizing the composition by autoclaving.

54. (no change) A method of providing a hematinic agent for treating a subject deficient in iron comprising the steps of:

formulating a composition which is a carboxymethylated reduced coated ultrasmall iron oxide colloid; and

terminally sterilizing the composition by autoclaving.

55. (no change) A method according to claim 53 or 54, having the further step of providing the autoclaved composition in a unit dosage.

56. (cancel) A kit containing multiple dosages of [~~the~~] an agent prepared by the method of claim 55.

57. (twice amended) An improved method of the type for [~~obtaining~~] administering a pharmacological polysaccharide composition [~~for pharmacological use from a polysaccharide wherein there is a risk of edematous response~~], wherein the improvement comprises prior to administering:

reducing [~~and carboxylating~~] the polysaccharide; and

[in] carboxylating[, providing] to an extent [~~of carboxylation~~] sufficient to produce a decreased edematous response to the [~~obtained carboxyalkylated~~] administered polysaccharide composition in comparison to [~~method for providing a~~] an edematous response to an administered unreduced uncarboxyalkylated polysaccharide [~~composition for pharmacological use obtained from an unmodified polysaccharide~~].

58. (once amended) A method according to claim 57, wherein the [~~pharmacological use is in vivo administration~~] method further comprises:

administering the reduced carboxyalkylated pharmacological polysaccharide composition to a mammalian subject as a plasma extender.

59. (once amended) An improved method of the type for obtaining a composition for pharmacological use from a dextran, wherein the improvement comprises:

reducing [~~and carboxymethylating~~] the dextran; and,

[~~in~~] carboxymethylating the dextran[, providing] to provide an extent of carboxymethylation sufficient to produce decreased edematous response to the [~~obtained carboxymethylated~~] administered dextran composition in comparison to [~~a method for obtaining a~~] an edematous response to an administered unreduced uncarboxyalkylated polysaccharide [~~composition for pharmacological use from an unmodified dextran~~].

60. (once amended) A method according to claim [~~59~~] 57, having the further step [~~after the reacting step,~~] of sterilizing the [~~carboxymethylated~~] carboxyalkylated reduced dextran composition.

61. (no change) A method according to claim 60, having the further step after the sterilizing step of providing the sterile composition as a single dosage unit.

62. (no change) A method according to claim 60, having the additional step of administering the composition to a mammal in need of a plasma extender.

63. (no change) A product for use as a plasma extender produced by the improved method of claim 60.

64. (once amended) A reduced [~~derivatized~~] carboxyalkylated polysaccharide iron oxide complex which is stable at a temperature of about 121 °C, wherein [~~the~~] a sodium salt of the complex does not contain an infrared absorption peak in the region of about 1650 cm^{-1} to about 1800 cm^{-1}.

65. (cancel) A reduced derivatized polysaccharide iron oxide complex according to claim 64, wherein the polysaccharide is carboxyalkylated.

66. (once amended) A reduced [~~derivatized~~] carboxyalkylated polysaccharide iron oxide complex according to claim 64, wherein the polysaccharide is [~~carboxyalkylated~~] carboxymethylated.

01275/00190 220684.1

Look at Marino!!

dependents on 1